

such as KDEL (SEQ ID NO:8) and REDL (SEQ ID NO:9). See Siegall, *et al.*, *J. Biol. Chem.* 264:14256 (1989). In a preferred embodiment, the cytotoxic fragment of PE retains at least 50%, preferably 75%, more preferably at least 90%, and most preferably 95% of the cytotoxicity of native PE. In a most preferred embodiment, the cytotoxic fragment is more toxic than native PE.--

✓ Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 4, at the end of the application.

REMARKS

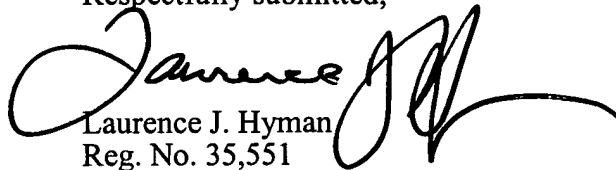
The Sequence Listing submitted herewith contains a correction of the SS scFv amino acid sequence provided in Figure 1. Figure 1 shows the one-letter code "L", or leucine, at position 21, whereas the correct amino acid at this position is actually isoleucine, or "I". Justification for this correction may be found on page 41, lines 9-11, where a description of the amino acid sequence shown in Figure 1 states that it is "obtained from translation of the nucleotide sequence of SS scFv", followed by the GenBank Accession Number AF35617 for said nucleotide sequence. The Sequence Listing includes the SS scFv nucleotide sequence from GenBank Accession Number AF35617 as SEQ ID NO:1, where the nucleotides at positions 61-63, *i.e.*, "ata", encode the amino acid "I", or isoleucine. The amino acid translation of this nucleotide sequence, also shown in GenBank Accession Number AF35617, contains an "I" at the appropriate position 21. Therefore, correction of this error of a typographical nature introduces no new matter. Correction of the Formal Drawing for Figure 1 to reflect this change will follow at an appropriate time.

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-9, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,


Laurence J. Hyman
Reg. No. 35,551

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
LJH:dmw

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 9 of page 6 has been amended as follows:

Figure 1: Figure 1 contains the amino acid sequence of SS scFv (SEQ ID NO:5) as deduced from its nucleotide sequence (SEQ ID NO:1). In the scFv, V_H is connected to V_L by a linker peptide, GVGGSG₄SG₄S (SEQ ID NO:6). The framework regions and CDRs have been marked.

Paragraph beginning at line 9 of page 18 has been amended as follows:

While the V_H and V_L regions of some antibody embodiments can be directly joined together, one of skill will appreciate that the regions may be separated by a peptide linker consisting of one or more amino acids. Peptide linkers and their use are well-known in the art. See, *e.g.*, Huston, *et al.*, *Proc. Nat'l Acad. Sci. USA* 8:5879 (1988); Bird, *et al.*, *Science* 242:4236 (1988); Glockshuber, *et al.*, *Biochemistry* 29:1362 (1990); U.S. Patent No. 4,946,778, U.S. Patent No. 5,132,405 and Stemmer, *et al.*, *Biotechniques* 14:256-265 (1993), all incorporated herein by reference. Generally the peptide linker will have no specific biological activity other than to join the regions or to preserve some minimum distance or other spatial relationship between them. However, the constituent amino acids of the peptide linker may be selected to influence some property of the molecule such as the folding, net charge, or hydrophobicity. Single chain Fv (scFv) antibodies optionally include a peptide linker of no more than 50 amino acids, generally no more than 40 amino acids, preferably no more than 30 amino acids, and more preferably no more than 20 amino acids in length. In some embodiments, the peptide linker is a concatamer of the sequence Gly-Gly-Gly-Ser (SEQ ID NO:7), preferably 2, 3, 4, 5, or 6 such sequences. However, it is to be appreciated that some amino acid substitutions within the linker can be made. For example, a valine can be substituted for a glycine.

Paragraph beginning at line 3 of page 29 has been amended as follows:

In preferred embodiments of the present invention, the toxin is *Pseudomonas* exotoxin (PE). The term "*Pseudomonas* exotoxin" as used herein refers to a full-length native (naturally occurring) PE or a PE that has been modified. Such modifications may include, but are not limited to, elimination of domain Ia, various amino acid deletions in domains Ib, II and III, single amino acid substitutions and the addition of one or more sequences at the carboxyl terminus such as KDEL (SEQ ID NO:8) and REDL (SEQ ID NO:9). See Siegall, *et al.*, *J. Biol. Chem.* **264**:14256 (1989). In a preferred embodiment, the cytotoxic fragment of PE retains at least 50%, preferably 75%, more preferably at least 90%, and most preferably 95% of the cytotoxicity of native PE. In a most preferred embodiment, the cytotoxic fragment is more toxic than native PE.